REMARKS/ARGUMENTS

Claims 1-18 are pending in the application. Claim 15 has been amended to recite an "EMMPRIN monoclonal antibody". Claim 18 has been canceled.

The Rejections Under 35 USC 112

The rejection of Claim 18 is rendered moot by the cancellation of the claim.

Claim 15 were rejected under 35 USC 112, first paragraph because, in the Examiner's view, the specification, while being enabling for a method of treating an angiogenesis dependent disease comprising administering an anti-EMMPRIN antibody where the disease is cancer; was not enabling for any "EMMPRIN antagonist". While applicants disagree with the Examiner's view, the rejection is rendered moot by the amendment of claim 15 to recite "EMMPRIN monoclonal antibodies".

The Rejection Under 35 USC 102 and 103

1. Claims 1, 3-4, 7, 13-15 and 18 were rejected under 35 USC 102(b) as being anticipated by WO 02/13763.

According to the Examiner, the WO'763 patent publication discloses a method of treating tumor growth or metastasis in a patient comprising administering EMMPRIN antagonist such as an anti-EMMPRIN antibody and therefore anticipates the claimed invention. Applicants respectfully disagree that the reference anticipates the claimed invention.

A patent claim "cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled". Elan Pharm. Inc v. Mayo Found., 346 F.3d 1051, 1054 (Fed. Cir. 2003). Since the how to use prong of Section 112 incorporates as a matter of law the requirement of 35 USC 101 that the specification disclose as a matter of fact a practical utility for the invention, In re Cortright, 165 F. 3d. 1353, 1356 (Fed. Cir. 1999), utility must be disclosed and supported to satisfy section 112 enablement requirements for a reference to be enabling. Mere plausibility is not the test for enablement under Section 112, one skilled in the art would have to believe from the disclosure that the compound would be effective in treating cancer. Where there is "no indication that one skilled in the art would accept without question statements [as to the effects of claimed drug products] and no evidence has been presented to demonstrate that the claimed products have those effects" an applicant, (and therefore an anticipatory reference) has failed to demonstrate sufficient utility and therefore cannot establish enablement. See In re Novak, 49 CCPA 1283, 306 F.2d 924, 928 (CCPA 1962).

The claimed invention is directed to a method of treating an angiogenesis-dependent disease in a mammal in need thereof comprising administering to the mammal an EMMPRIN

monoclonal antibody or fragment thereof in an amount effective to inhibit angiogenesis. The reference does not disclose or suggest treating an angiogenesis dependent disease and does not disclose any information concerning angiogenesis or how to determine an angiogenesis inhibiting amount of the antibody. The publication only contains a general reference to treating cancer with an anti-EMMPRIN antibody, but contains absolutely no data to support it. It is nothing more than speculation, mere plausibility, based on the fact that, in a prior publication, EMMPRIN expressing tumor cells had been shown to up-regulate the expression of MMPs in fibroblasts co-cultured therewith. See page 57 of WO'763. There is absolutely no data showing that inhibiting EMMPRIN can have an effect on tumor angiogenesis; or that anti-EMMPRIN antibodies or any other anti-EMMPRIN constructs can in fact inhibit tumor growth or metastases. A showing that EMMPRIN expressing tumor cells up-regulate matrix metalloproteinases is a long way from demonstrating that inhibiting EMMPRIN can inhibit tumor growth or metastases. One skilled in the art would not draw the conclusion that blocking EMMPRIN would inhibit tumor growth from the cited reference. There is simply no biological data using EMMPRIN antibodies and no biological data in an angiogenesis or tumor model of any kind. Therefore, the reference is completely lacking in enablement. One skilled in the art would recognize it for what it is; mere speculation.

Even if one were to assume that the claimed method of inhibiting angiogenesis and the disclosure of treating cancer were inherently the same as the Examiner states, the reference simply is not enabling for the cancer treatment claim. The Examiner asserts that the reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of the invention and such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his own knowledge to make the claimed invention, citing In re Donohue, 76 F.2d 531 (Fed. Cir. 1985). However, it is Applicant's position that the reference does not in fact demonstrate possession of the invention and one skilled in the art would recognize that the reference does not disclose any data from which one could reasonably have concluded that the reference demonstrated possession of the claimed method of inhibiting tumor growth, even if one skilled were to apply his own knowledge. Cancer treatment is just not that predictable. A mere statement that an antibody would be useful in treating cancer without any supporting data demonstrating such in an in vivo model simply cannot be an enabling disclosure for a cancer treatment claim. Accordingly, the conclusion that the cited reference is not enabling is inescapable and the rejection should be withdrawn.

2. Claims 1, 5-6, 9 and 13-17 were rejected under 35 USC 103(a) as being unpatentable over WO'763 in view of US Patent 6,406,693.

As stated previously, the rejection should be withdrawn because neither cited reference fairly teaches or suggests the method of the invention. Neither reference discloses or suggests that EMMPRIN antibodies could be used in a method for treating cancer or inhibiting tumor growth. As stated above, WO'763 is not an enabling reference for the claimed method. The '693 patent contains disclosures about using antibodies to inhibit angiogenesis and treat cancer, but does not teach anything at all about anti-EMMPRIN antibodies. The Examiner asserts that the '693 patent teaches that certain anti-angiogenic therapies have been shown to cause tumor regression (citing the alphaVbeta3 antibody LM609) and therefore it would have been obvious to combine the LM609 antibody with the anti-EMMPRIN antibody as taught by the '763 publication in a method of treating an angiogenesis dependent disease such as tumor growth and metastases. Applicant does not understand the logic of this rejection since neither reference teaches the claimed use of anti-EMMPRIN antibodies in the method of treating an angiogenesis dependent disease such as tumor growth and metastases in the first place. If the claim were to a combination of such antibodies where the use of anti-EMMPRIN antibodies in such a method was already known, the combination indeed would be obvious. But that is not the case here. The use of EMMRIN antibodies in the angiogenesis mediated treatment of cancer was not already known so the teaching of the '693 patent concerning other antibodies does not render the claimed method obvious. Moreover, only claim 16 relates to the combination with other anti-angiogenesis agents and that is not obvious unless there is a disclosure that suggests the use of EMMPRIN antibodies in the method of the invention in the first place. For the reasons stated above, no such disclosure exists in this case. Accordingly, Applicant simply does not see how the combination of the references makes the use of EMMPRIN antibodies in the claimed method obvious when there is no enabling disclosure for the method anywhere in the cited references. The '693 patent simply does not teach or suggest anything that would be relevant to anti-EMMPRIN antibodies and their use in inhibiting angiogenesis in a tumor, unless one already knew that the antibodies would be useful for that purpose. Thus, because the WO'763 patent does not fairly teach or suggest the method of the invention, and the '693 patent is not relevant to EMMPRIN antibodies, the combination does not render the claimed invention obvious and the rejection should be withdrawn.

3. Claims 1, 4-7, 13-15 and 18 are rejected under 35 USC 103(a) as being unpatentable over Looksmart publication 2001 in view of Sameshima et al.

As stated previously, it is Applicant's position that the Looksmart publication simply does not fairly disclose or suggest the claimed invention. Looksmart merely shows that breast cancer cells transfected with GFP-EMMPRIN produce larger tumors and that EMMPRIN can stimulate production of MMPs 1, 2 and 3. It does not teach that EMMPRIN has a direct role in angiogenesis; does not teach or suggest the use of an EMMPRIN monoclonal antibody; and does not teach or suggest that the use of EMMPRIN antibodies can inhibit angiogenesis. As stated above, a patent claim cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled. Neither Looksmart nor Dameshima et al are enabling for the claimed method.

These reports that cells transfected with EMMPRIN responded by producing more MMPs, are generally limited to in vitro studies, and were at best only indirect evidence suggesting EMMPRIN may be linked to angiogenesis. In many cases, the purity of EMMPRIN purified from the cancer cells was not determined. Therefore, it is very likely that other pro-angiogenic factors could have been co-purified with EMMPRIN and were accountable for the stimulation in endothelial cells observed. Unless the investigators could show that the effect of purified EMMPRIN on endothelial cells can be neutralized by anti-EMMPRIN antibodies, their findings were not confirmed. In the Looksmart publication, antisense cDNA and ribozyme constructs failed to block EMMPRIN expression and were inactive in vitro. So there is no evidence that blocking EMMPRIN would have any effect on angiogenesis.

Accordingly, the reference is at best a teaching that EMMPRIN transfected cells produce larger tumors. There is no direct evidence that EMMPRIN has a role in angiogenesis. Even if the reference could be fairly read to suggest that EMMPRIN stimulates tumor angiogenesis in vivo, which the publication does not, it would still be necessary to show with either antibody or antisense (like applicants did) that inhibiting EMMPRIN suppresses tumor angiogenesis to render the claimed invention unpatentable. The present application contains direct evidence showing:

a. Inhibiting EMMPRIN expression in tumors with anti-sense construct ("EMMPRIN antagonists") directly suppressed tumor angiogenesis in vivo, quantitatively measured by CD31 staining;

b. That inhibiting EMMPRIN led to suppression of VEGF production, a key angiogenic factor, both in vitro and in vivo. This finding is novel and clearly differentiates

applicant's findings from others concerning the relationship between EMMPRIN and MMP.

Likewise, the Sameshima et al reference merely shows that EMMPRIN stimulates production of MMP-2 activators, and that anti-EMMPRIN antibodies can inhibit MT2-MMP production. This does not show that EMMPRIN has an angiogenic effect or that EMMPRIN antibodies can inhibit angiogenesis directly or that they have any effect on tumors.

Accordingly, the cited references fail to render the claimed invention obvious and the rejection should be withdrawn.

4. Claim 3 was rejected under 35 USC103(a) over Looksmart in view of Sameshima in further view of Owens et al.
Looksmart and Sameshima are discussed above. Owens et al is cited for its disclosure of antibody fragments. Because Looksmart and Sameshima do not render the claims obvious, the addition of Owens et al does not add anything to the rejection.

5. Claims 9 and 16-17 are rejected under 35 USC 103(a) as being unpatentable over Looksmart in view of Sameshima as applied to claims 1-2, 4-6, 8, 13-15 and 18 above and further in view of the '693 patent.

Looksmart and Sameshima are discussed above. The '693 patent is applied for the rejection over claim 9, which recites angioma, and claims 16 and 17 which recite the combination with other anti-angiogenic agents. Because the primary references, Looksmart and Sameshima, do not fairly teach or suggest the claimed method, the addition of the '693 patent for other anti-angiogenic agents, does not cure the deficiency in the rejection. It should therefore be withdrawn.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

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